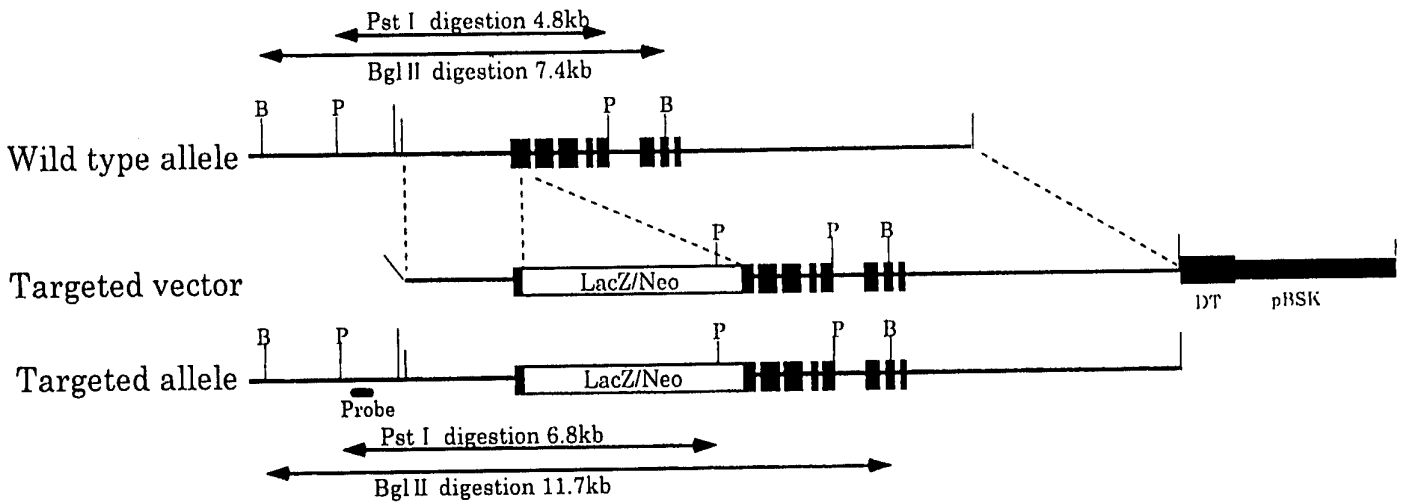
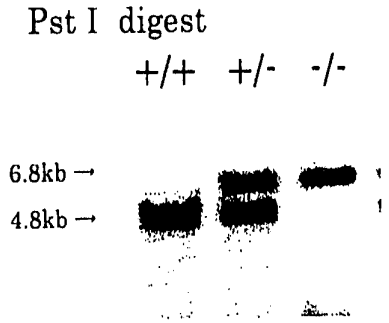
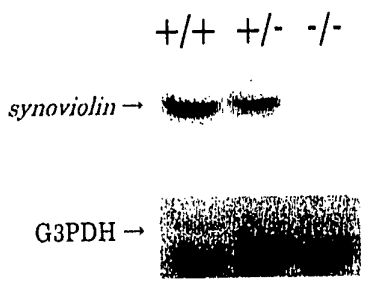
FIG. 1 GENERATION OF SYNOVIOLIN KO MICE



Southern blot



Northern blot



Western blot

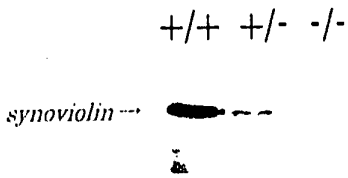


FIG. 2 BIRTH OF SYNOVIOLIN KO MICE

Stage	Total (Litters)	*synoviolin* +/+	*synoviolin* +/-	*synoviolin* -/- (alive)	*synoviolin* -/- (dead)
Postnatal	10 (2)	2	8	0	
E18.5	3 (1)	3	0	0	
E17.5	4 (1)	0	4	0	
E15.5	5 (1)	1	4	0	
E14.5	50 (8)	22	22	0	6
E13.5	81(13)	27	47	2	5
E12.5	104(17)	26	67	10	1
E11.5	35 (5)	8	18	8	1
E10.5	26 (4)	8	12	6	0
Total	318(51)	97	182	39	

FIG. 3 PHENOTYPES OF SYNOVIOLIN KO MICE

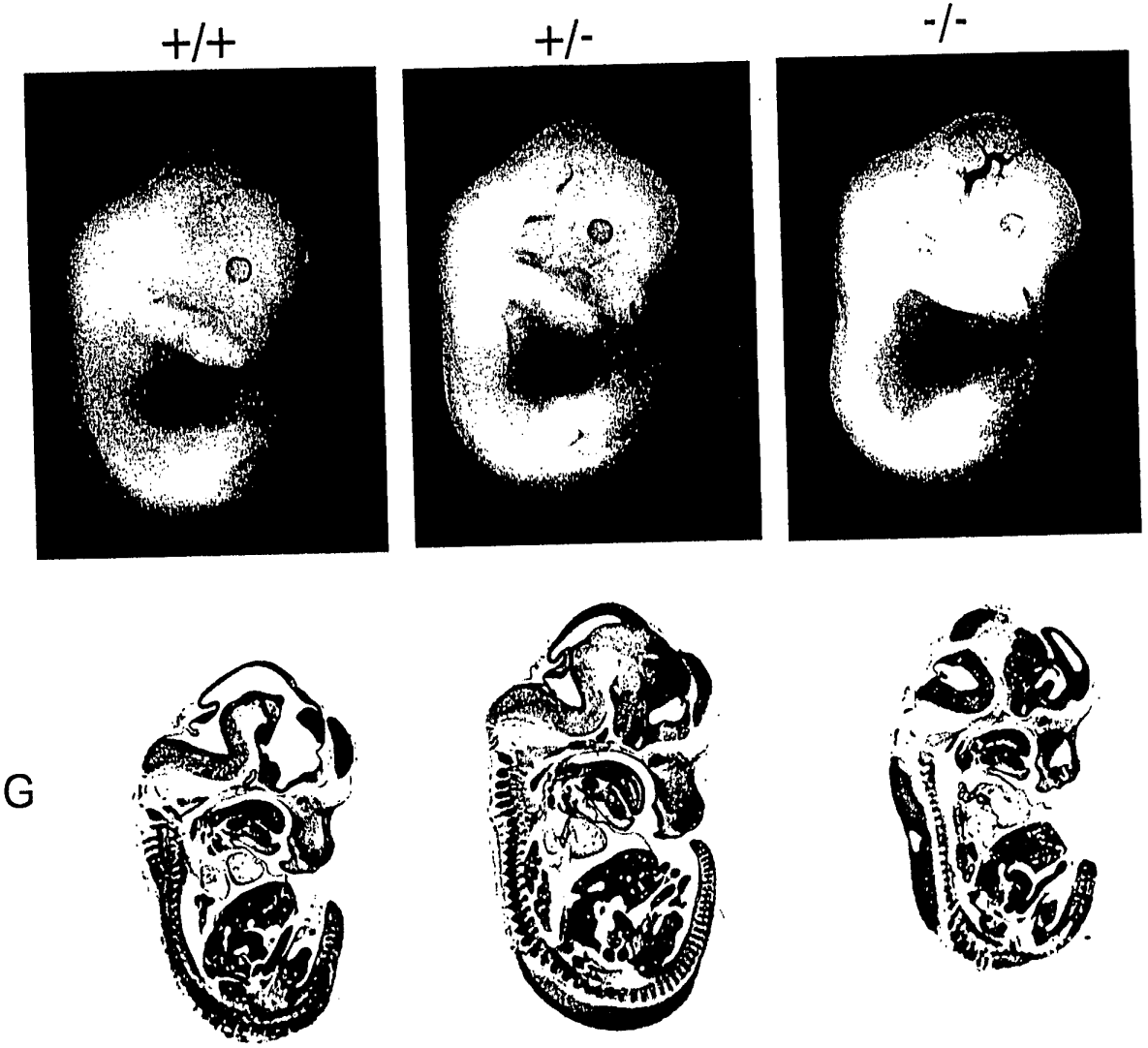


FIG. 4 PHENOTYPES OF SYNOVIOLIN KO MICE

(HE STAINING)

Liver (×400)

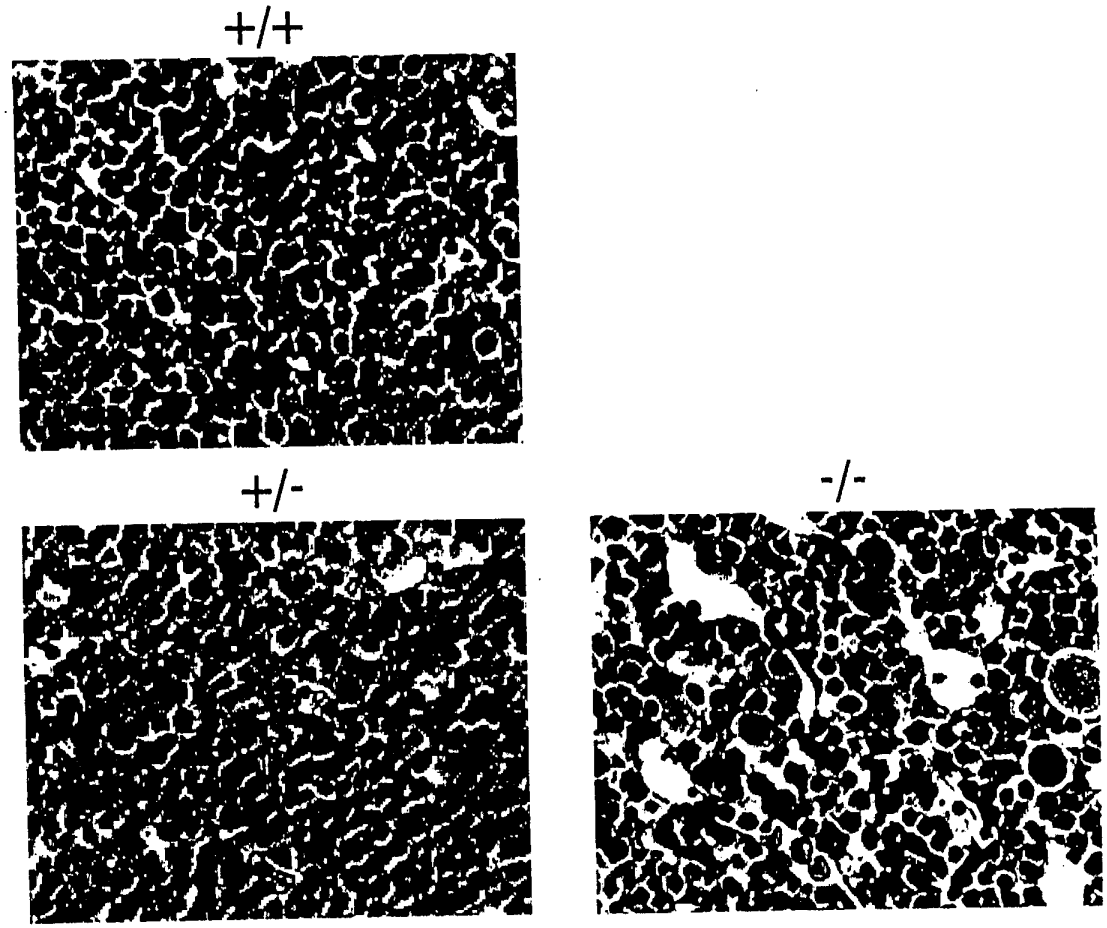


FIG. 5 KO MICE EXPERIENCING EMBRYONIC DEATH AT AROUND E13.5

Gene	Stage	Phenotype
AML1	E12.5	Abnormal secondary hematopoiesis in fetal liver
Angiopoietin-1	E12.5	Abnormal cardiovascular system
bcl-x	E13.0	Cell death in the peripheral ganglia, and increased cell death of immature hematopoietic cells in fetal liver
cas	E11.5-12.5	Congestion due to systolic dysfunction of vascular smooth muscles, and cardiac hypoplasia
EKLF	up to E13.0	Extreme anemia
EPO	E13.0	Abnormal secondary hematopoiesis in fetal liver
EPOR	E13.0	Abnormal secondary hematopoiesis in fetal liver
c-jun	E11.5-15.5	Increase of nucleated erythrocytes in fetal liver
keratin-8	E12.0-15.5	Increase of nucleated erythrocytes in fetal liver
c-myb	E15.5	Abnormal secondary hematopoiesis in fetal liver
RB	E12.0-16.0	Abnormal central nervous system, and abnormal hematopoietic system
sox4	E14.0	Cardiac malformation
Tie-1	E13.5-14.5	Abnormal maintenance of vascular cells
VCAM-1	E11.5-12.5	Placental and cardiac malformation

Excerpt from Knockout Mice Data Book

FIG. 6 INVESTIGATION OF PRIMARY HEMATOPOIESIS (GIEMSA STAINING)

10.5 d.p.c.

Peripheral blood (×100)

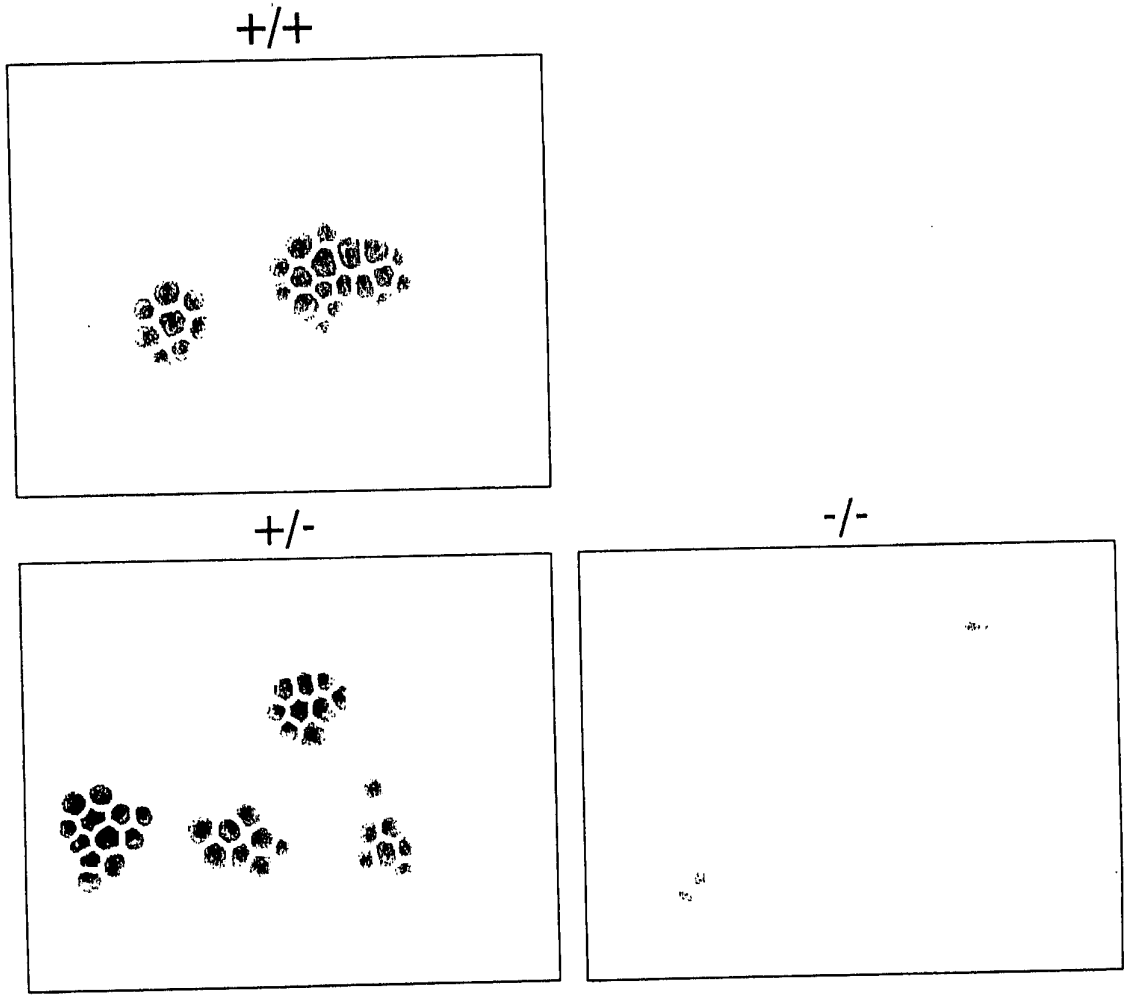
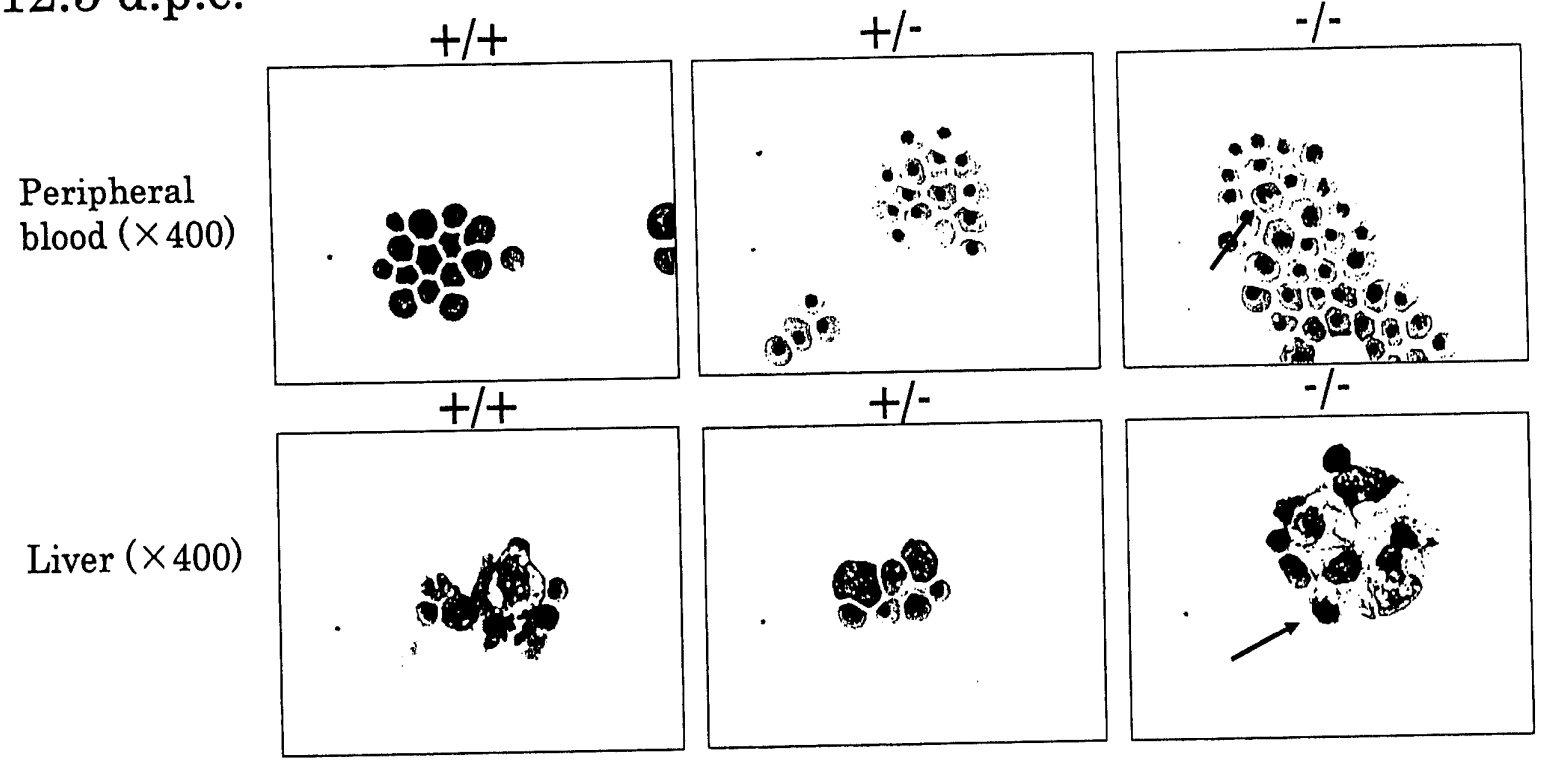


FIG. 7 INVESTIGATION OF SECONDARY HEMATOPOIESIS (GIEMSA STAINING)

12.5 d.p.c.



Erythroblast morphology	+/+	+/-	-/-
Nuclear disruption	0.0%	0.6%	2.0%
Binucleation	0.1%	1.2%	2.1%
Howell-Jolly body	1.7%	3.8%	6.4%

Mϕ phagocytosis image	+/+	+/-	-/-
(cells/ 100 Mϕ)	1	7	22

FIG. 8 HEMOPHAGOCYTOSIS IN SYNOVIOLIN KO MICE

Liver (×400)

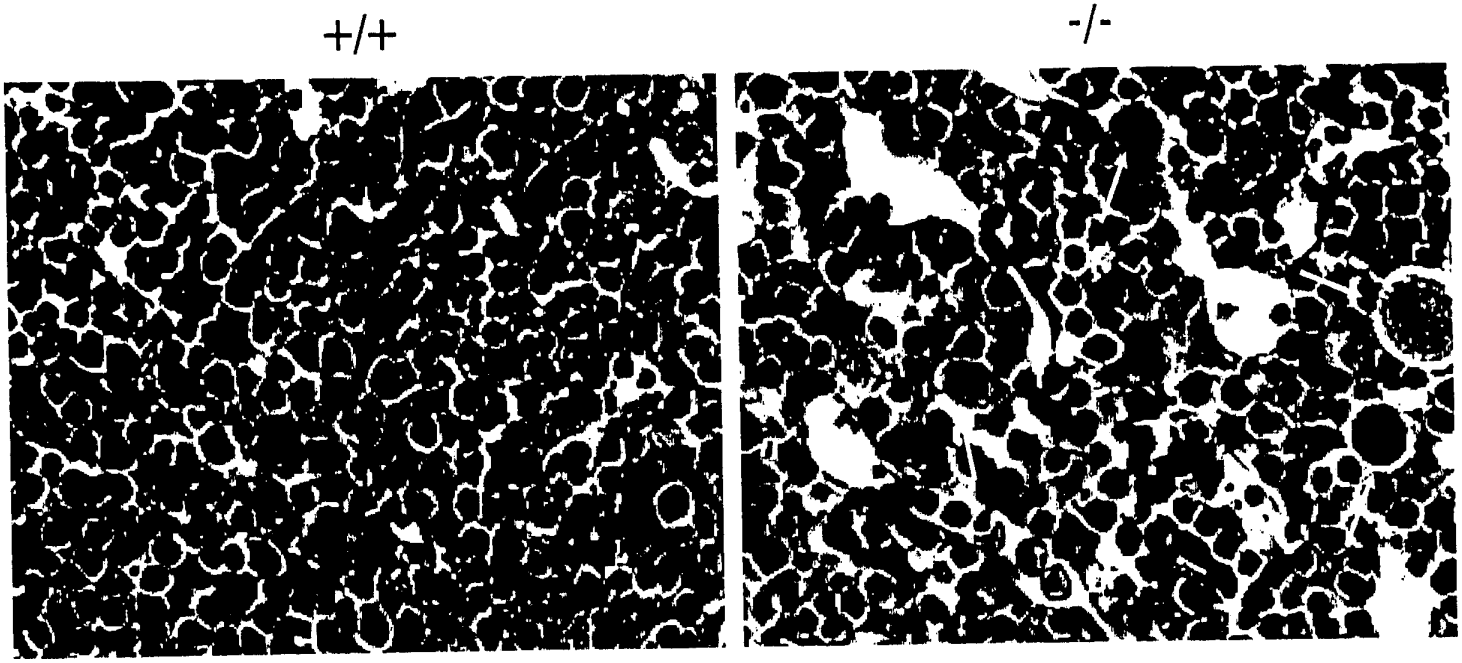


FIG.9

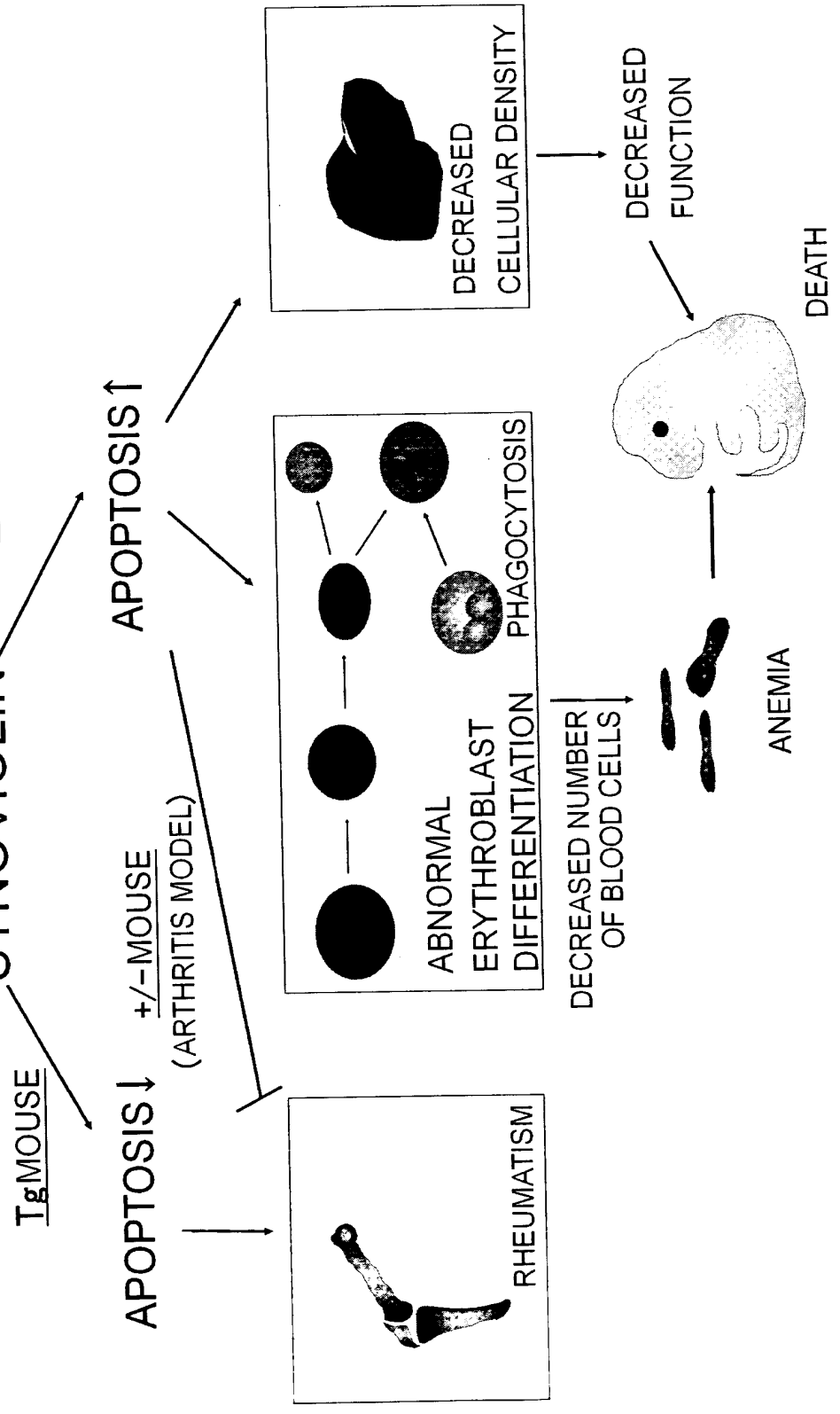

SYNOVIOLIN
TgMOUSE
KO MOUSE
APOPTOSIS↓
APOPTOSIS↑
+/−MOUSE
(ARTHRITIS MODEL)
RHEUMATISM
ABNORMAL
ERYTHROBLAST
DIFFERENTIATION
PHAGOCYTOSIS
DECREASED NUMBER
OF BLOOD CELLS
ANEMIA
DECREASED
CELLULAR DENSITY
DECREASED
FUNCTION
DEATH

Table 1

Table 1. Genotypes of Offsprings from *syno*$^{+/-}$ Intercrosses

Stage	Total (Litters)	*syno* +/+	*syno* +/-	*syno* -/- (alive)	*syno* -/- (dead)
Postnatal	10 (2)	2	8	0	
E18.5	3 (1)	3	0	0	
E17.5	4 (1)	0	4	0	
E15.5	5 (1)	1	4	0	
E14.5	50 (8)	22	22	0	6
E13.5	81 (13)	27	47	2	5
E12.5	104 (17)	26	67	10	1
E11.5	35 (5)	8	18	8	1
E10.5	26 (4)	8	12	6	0
Total	318 (52)	97	182	39	

Surviving embryos were defined as those with beating hearts at time of dissection.

Figure.1

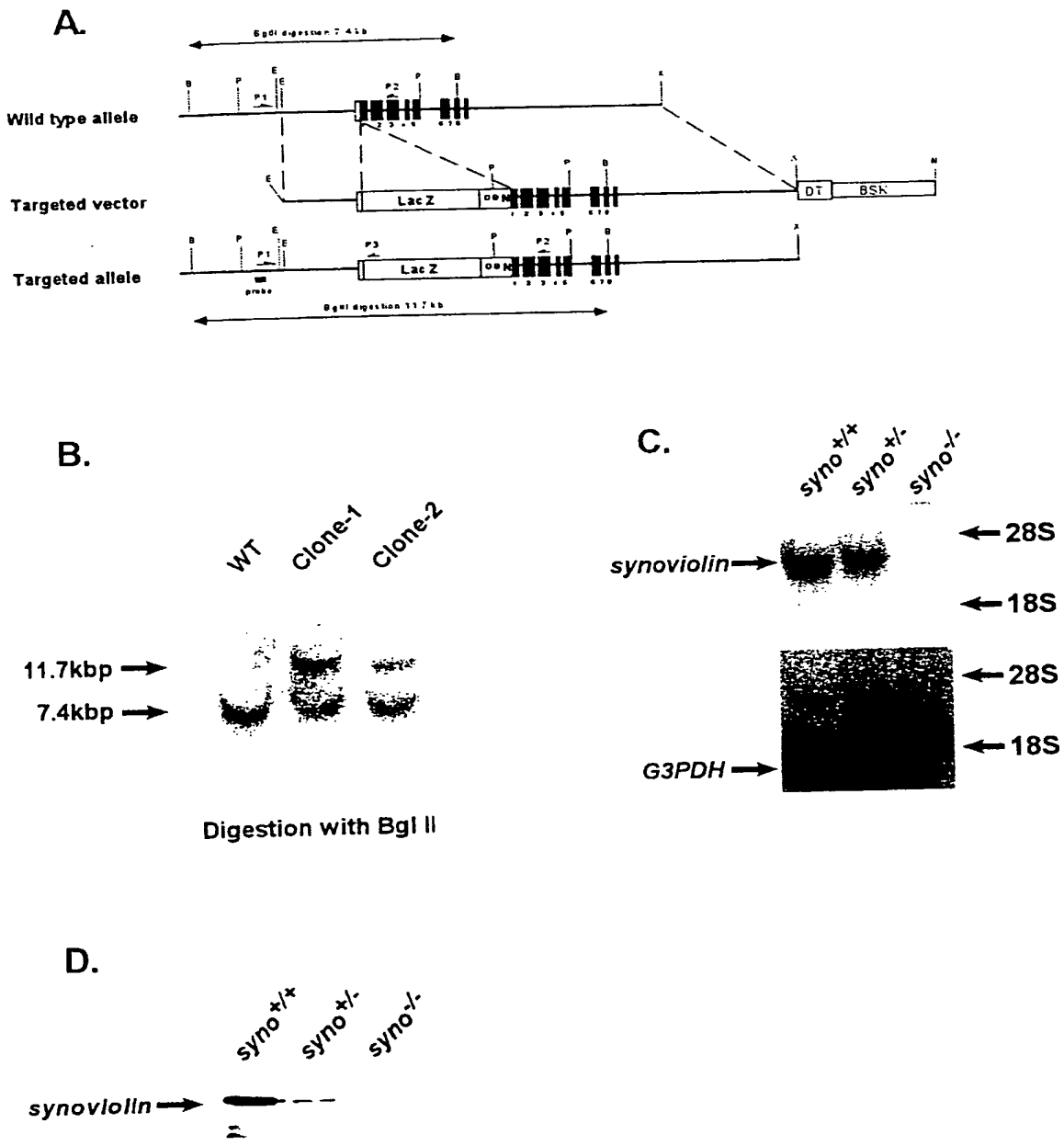

A.
Wild type allele
Targeted vector
Targeted allele
Lac Z
DT
BSK
probe
B.
WT
Clone-1
Clone-2
11.7kbp
7.4kbp
Digestion with Bgl II
C.
syno+/+
syno+/-
syno-/-
synoviolin
28S
18S
28S
18S
G3PDH
D.
syno+/+
syno+/-
syno-/-
synoviolin

Figure.2

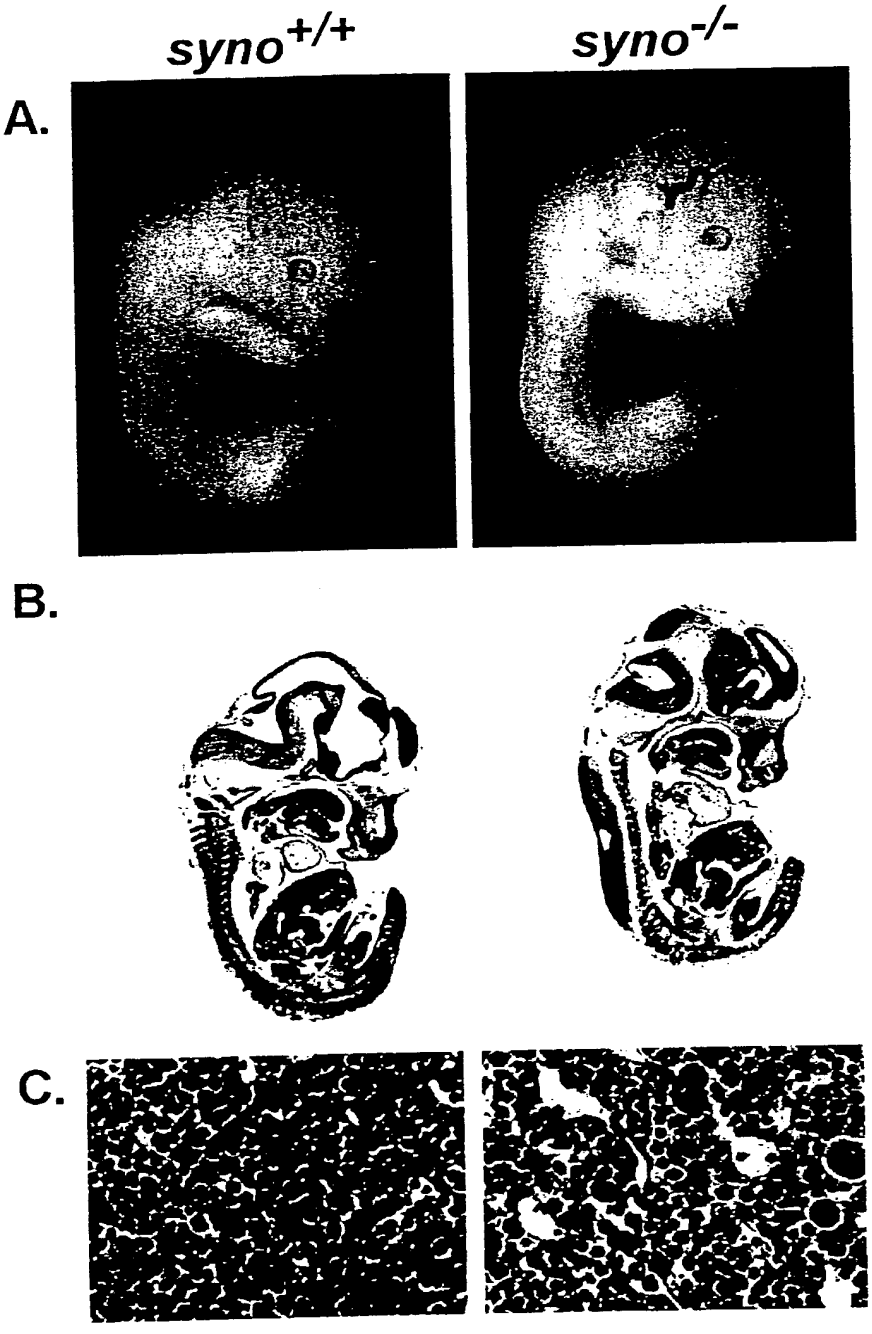


Figure.3

Figure.4

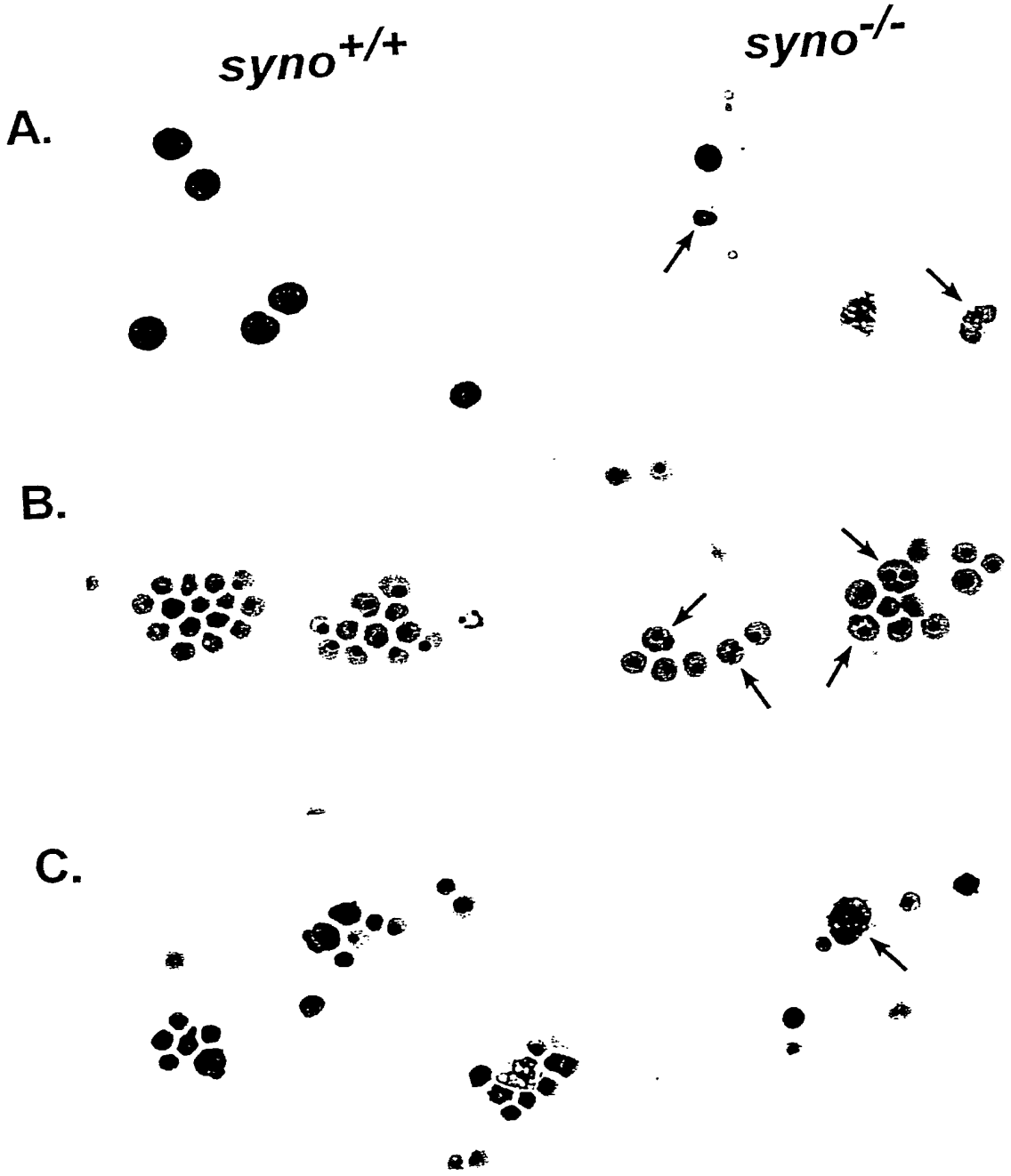


Figure.5

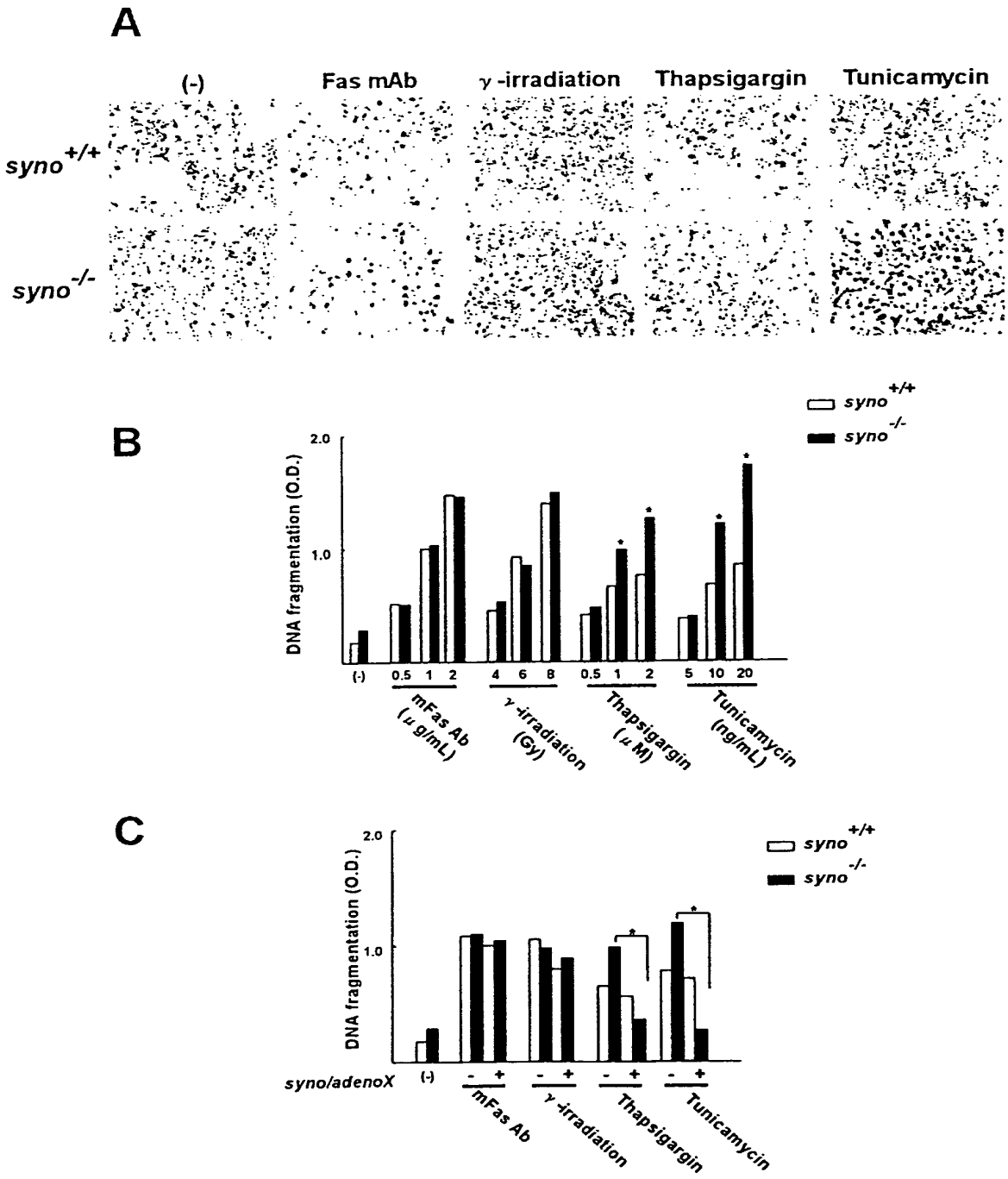
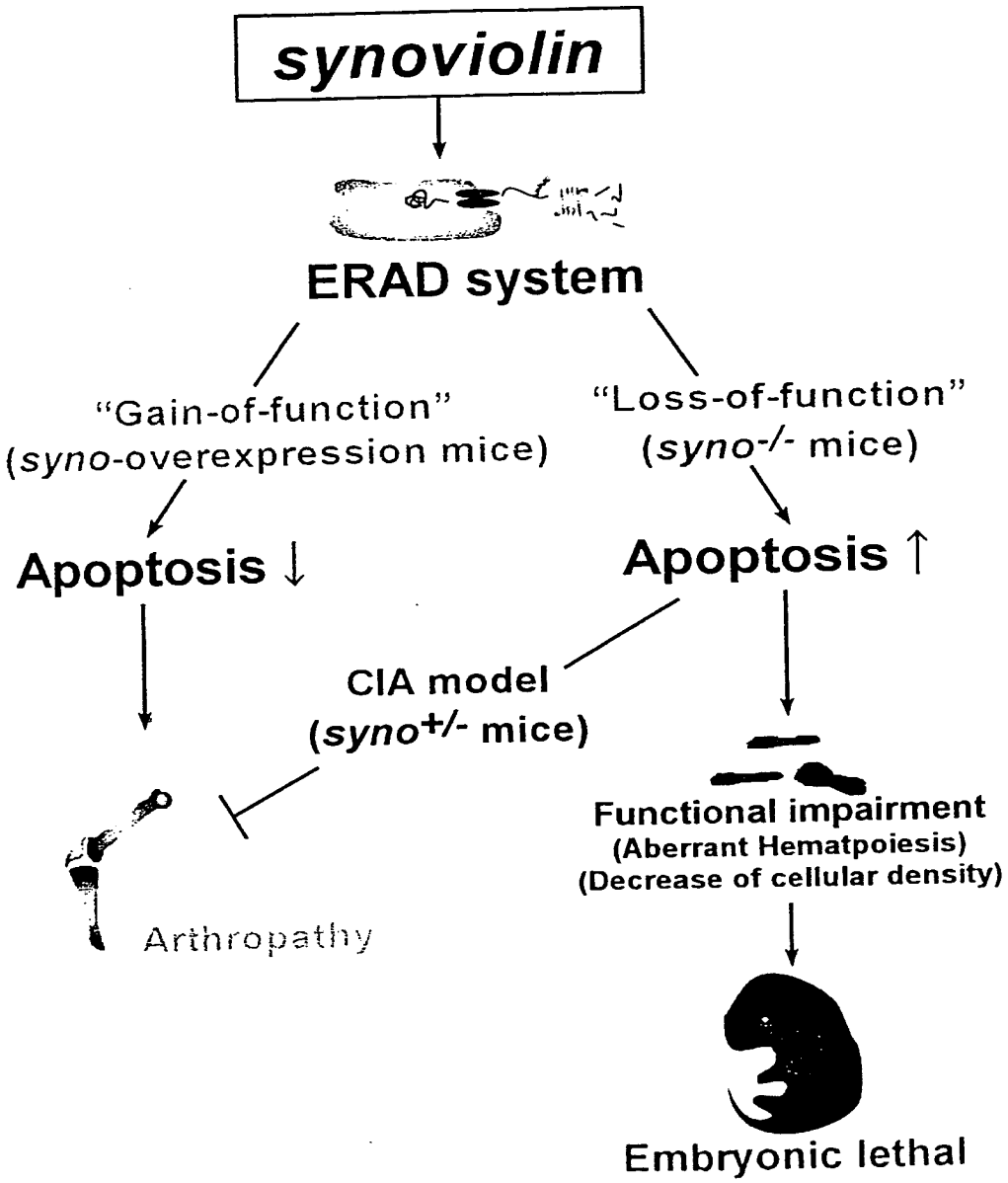

A
(-)
Fas mAb
γ -irradiation
Thapsigargin
Tunicamycin
syno+/+
syno-/-
B
syno+/+
syno-/-
DNA fragmentation (O.D.)
2.0
1.0
(-)
0.5 1 2
4 6 8
0.5 1 2
5 10 20
mFas Ab (μg/mL)
γ -irradiation (Gy)
Thapsigargin (μM)
Tunicamycin (ng/mL)
C
syno+/+
syno-/-
DNA fragmentation (O.D.)
2.0
1.0
syno/adenoX
(-)
- +
mFas Ab
γ -irradiation
Thapsigargin
Tunicamycin

Figure.6


synoviolin
ERAD system
"Gain-of-function"
(syno-overexpression mice)
"Loss-of-function"
(syno-/- mice)
Apoptosis ↓
Apoptosis ↑
CIA model
(syno+/- mice)
Arthropathy
Functional impairment
(Aberrant Hematpoiesis)
(Decrease of cellular density)
Embryonic lethal